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Applicant:
(Name and address)

7TM Pharma A/S
Rønnegade 2
DK-2100 København Ø
Denmark

Title: Quinoline compounds for use in mch receptor related disorders.

IPC: -

This is to certify that the attached documents are exact copies of the above mentioned patent application as originally filed.

Patent- og Varemærkestyrelsen
Økonomi- og Erhvervsministeriet

16 January 2004

Pia Petersen

PATENT- OG VAREMÆRKESTYRELSEN

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QUINOLINE COMPOUNDS FOR USE IN MCH RECEPTOR RELATED DISORDERS

Field of the invention

The present invention relates to use of quinoline compounds for the preparation of a pharmaceutical and/or a cosmetic composition for the treatment, prophylaxis and/or diagnosis of a condition caused by or involving a melanin-concentrating hormone. The quinoline compounds have been fount to interact with a melanin-concentrating hormone receptor, a MCH receptor. The compounds have modulating activity on the MCH receptor such as e.g. antagonistic, agonistic or allosteric activity and are useful for medicinal or cosmetic purposes such as, e.g. in the treatment or prevention of feeding disorders like obesity, metabolic syndrome, Type II diabetes, bulimia etc. or in the treatment or prevention of depression.

The invention also relates to therapeutic and/or prophylactic use of the compounds, to novel compounds and to processes for the preparation of the novel compounds, to pharmaceutical compositions comprising the compounds; to the manufacture of such compositions and to methods for the treatment and/or prevention of MCH receptor related disorders.

Background of the invention

Melanin-concentrating hormone (MCH) is a cyclic peptide that originally was isolated from salmoid pituitaries. In the fish, the 17 amino acid peptide causes aggregation of melanin and inhibits the release of ACTH. Mammalian MCH (19 amino acids) is highly conserved between rat, mouse and human exhibiting 100% amino acid identity. In the last decades there has been increasing activity in the research in the physiologic roles of MCH. It has been reported that MCH is involved in the feeding or body weight regulation, in energy balance, in response to stress, in water balance, in energy metabolism, in the general arousal/attention state, memory and cognitive functions and in psychiatric disorders. The biological effects of MCH are believed to be mediated by specific MCH receptors, and the MCH1 and MCH2 receptors have been described. Antagonists of MCH receptor (e.g. MCH1 receptor) may be suitable for use as obesity or weight reducing agents and they are also believed to have antidepressant and/or anxiolytic properties.

The present invention provides novel use of compounds that have been found to possess a MCH modulating activity, i.e. antagonistic, inverse agonistic/negative antagonism, allosteric modulator, partial agonist or agonistic action.

Detailed description of the invention

The term "alkenyl" is intended to indicate an unsaturated alkyl group having one or more double bonds.

The term "alkynyl" is intended to indicate an unsaturated alkyl group having one or more triple bonds.

The term "cycloalkyl" is intended to denote a cyclic, saturated alkyl group of 3-7 carbon atoms.

The term "cycloalkenyl" is intended to denote a cyclic, unsaturated alkyl group of 5-7 carbon atoms having one or more double bonds.

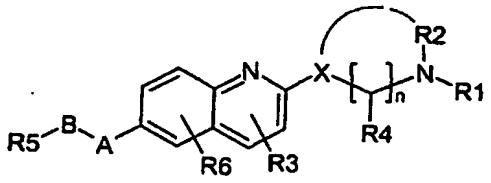
The term "alkoxy" is intended to indicate the group alkyl-O-.

The term "aryl" is intended to denote an aromatic (unsaturated), typically 6-membered, ring, which may be a single ring (e.g. phenyl) or fused with other 5- or 6-membered rings (e.g. naphthyl or indole).

The term "heteroaryl" is intended to denote an aromatic (unsaturated), 5- or 6-membered, ring, which may be a single ring (e.g. pyridyl) or fused with other 5- or 6-membered rings (e.g. quinoline or indole).

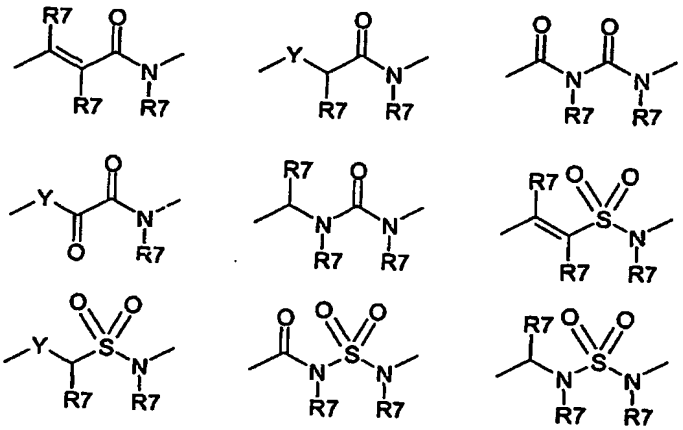
The term "heterocyclyl" is intended to indicate a cyclic unsaturated (heteroalkenyl), aromatic ("heteroaryl") or saturated ("heterocycloalkyl") group comprising at least one heteroatom.

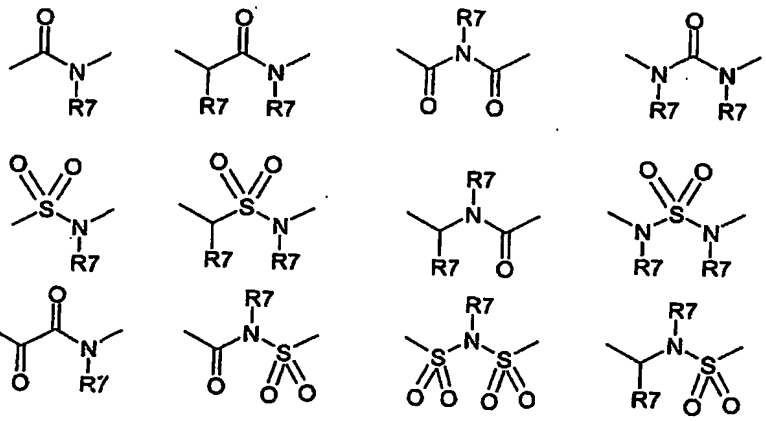
The present invention relates to the use of a compound with the following structure (Formula Ia)

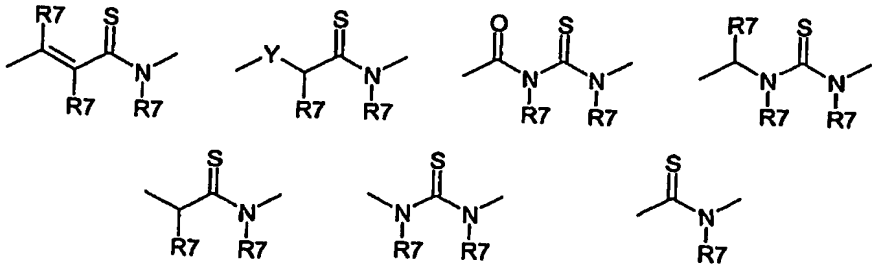


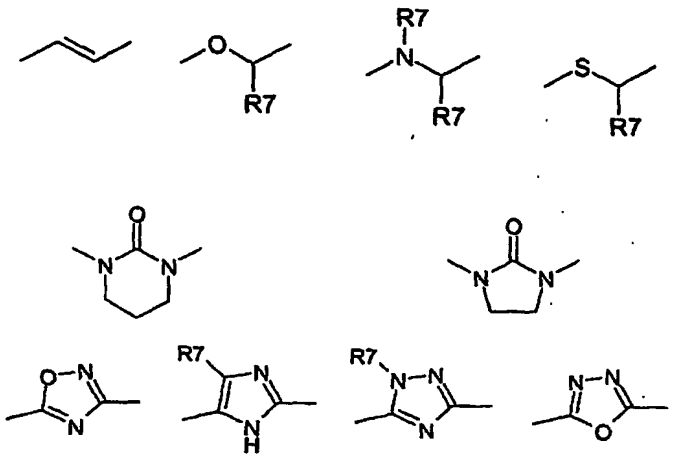
wherein the quinoline moiety may contain more than one nitrogen atom such as, e.g. 2 or 3 nitrogen atoms.

and wherein -A- is a linker, which is selected from the group consisting of









and, wherein the linker may be attached via either of the two free bonds to the B group;

and Y being CHR7, O, S, NR7;

and R7 is the same or different and is hydrogen or a straight or branched C_1-C_4 alkyl or alkenyl group; R7 can be linked direct or via hetero atoms to B or the quinoline ring system when chemically feasible;

and X being nitrogen, carbon, oxygen or sulphur and X being restricted to nitrogen or carbon when X linked to R2 as indicated in formula Ia;

B is an aryl or heteroaryl group such as, e.g. phenyl, pyridine, pyrimidine, pyrazine, thiophene, oxazole, isothiazole, pyrazole, pyrrole, imidazole, indole, benzimidazole, quinoline, isoquinoline, furan, benzofuran, benzothiophene, benzothiazole, indazole, thiazole, isoxazole, oxadiazole, indan;

R1 and R2 are the same or different selected from hydrogen, straight or branched alkyl, alkenyl or alkynyl groups with 1-6 carbon atoms; cycloalkyl groups with 3-7 carbons; alkylcycloalkyl with 4-8 carbons atoms; alkylaryl groups such as benzyl, 2-ethylphenyl, 3-propylphenyl; alkylheteroaryl groups; the alkyl, aryl and heteroaryl groups may be substituted with substituents such as Alk-CONH-, Alk-O-, HO-, NC-, AlkNH-, Alk_2N-, -$CONH_2$, -CONHAlk, -$CONAlk_2$, or the aryl and heteroaryl groups fused with moieties such as -O-CH_2-O-, -N=CH-NH-, -O-CH=N-;

Alk is the same or a different alkyl, alkenyl or alkynyl group;

R4 is the same or different and is hydrogen or a straight or branched C_1-C_4 alkyl group;

R3 may be selected from hydrogen, alkyl, alkenyl or alkynyl groups, halogen atoms, alkoxy groups (AlkO-), hydroxy, alkylamino groups (AlkNH-), dialkylamino groups (Alk_2N-), hydroxylalkyl groups, carboxamido groups (-$CONH_2$, -CONHAlk, -$CONAlk_2$), acylamido groups (-NHCO-Alk), acyl groups (-CO-Alk), -CHO, nitrile, -SCH_3, partially or fully fluorinated alkyl, alkoxy or thioalkoxy groups such as -CH_2CF_3, -CF_2CF_3, -CF_3, -OCF_3, -SCF_3; -SO_2NH_2, -SO_2NHAlk, -SO_2NAlk_2, -SO_2Alk;

R1, R2, R3 or R4 may optionally be linked to each other, when possible; and oxygen or nitrogen atoms may be inserted in the chain or ring in a chemically stable position;

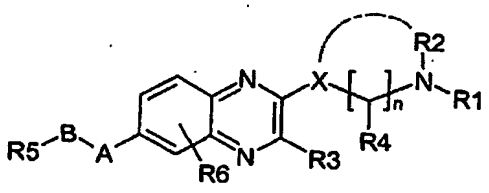
R5 is hydrogen, halogen atoms, alkyl, alkenyl or alkynyl groups, cycloalkyl groups with 3-7 carbons, aryl groups (Ar), heteroaryl groups, heterocyclyl groups, alkylcycloalkyl groups, alkylaryl groups, alkylheterocyclyl groups, alkylheteroaryl groups, arylalkoxy groups (e.g. $ArCH_2O$-), aryloxy groups (ArO-), arylamino groups (Ar-NR7-, ArNH-), arylalkylamino groups (ArAlkNH-, ArAlkNR7-, $ArCH_2NR7$-, $ArCH_2NH$-), alkoxy groups (AlkO-), alkylamino groups (AlkNH-), dialkylamino groups (Alk_2N-), -$CONH_2$, -CONHAlk, -CONHAr -$CONAlk_2$, -NHCO-Alk, -NHCO-Ar, -CO-Alk, -CO-Ar, -CF_2-Ar, -$N(CF_3)_2$, -SCH_3, partially or fully fluorinated alkyl, alkoxy or thioalkoxy groups such as -CH_2CF_3, -CF_2CF_3, -CF_3, -OCF_3, -SCF_3;

optionally, one or more R5 may be present on B; and

n is 0, 1, 2 or 3 with the proviso that
when n is 0 or 1 then X is C and
when n is 2 or 3, then X is C, O, S or N

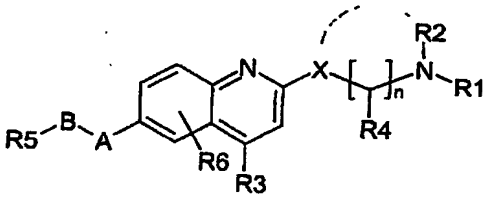
for the preparation of a pharmaceutical composition for the treatment, prophylaxis and/or diagnosis of a condition caused by or involving a melanin-concentration hormone.

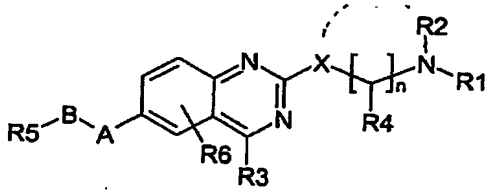
In another embodiment, the invention relates to the use of a compound that has the following structure (Formula Ib)



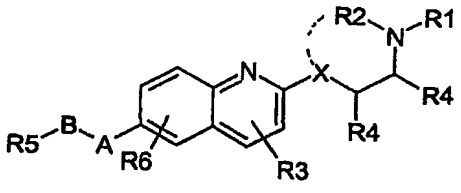
wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y, X and n are as defined above for the preparation of a pharmaceutical composition for the treatment, prophylaxis and/or diagnosis of a condition caused by or involving a melanin-concentration hormone.

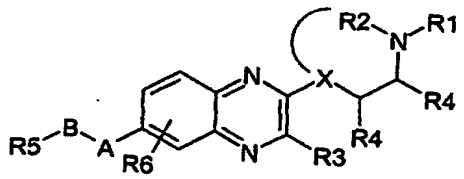
In a still further embodiment, the compound has one of the following structures:





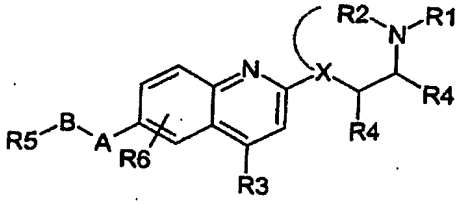
wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y, X and n are as defined above, or

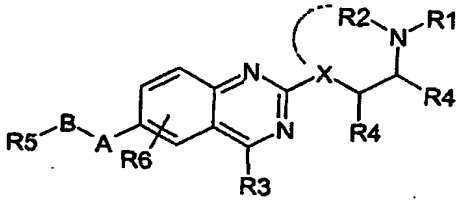


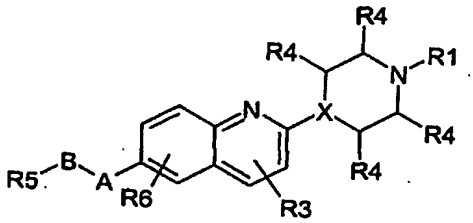


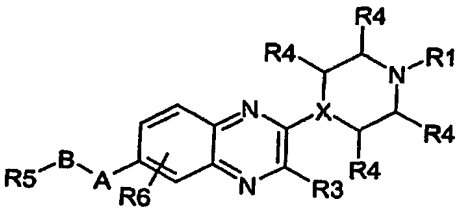
and wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined above.

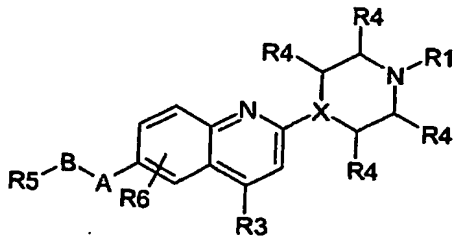
In another embodiment, the compound has one of the following structures:

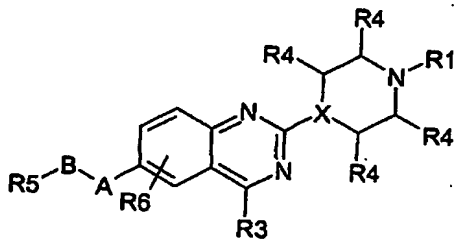








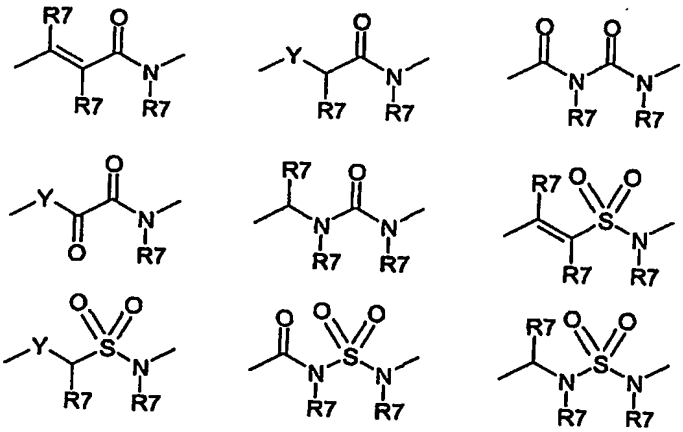




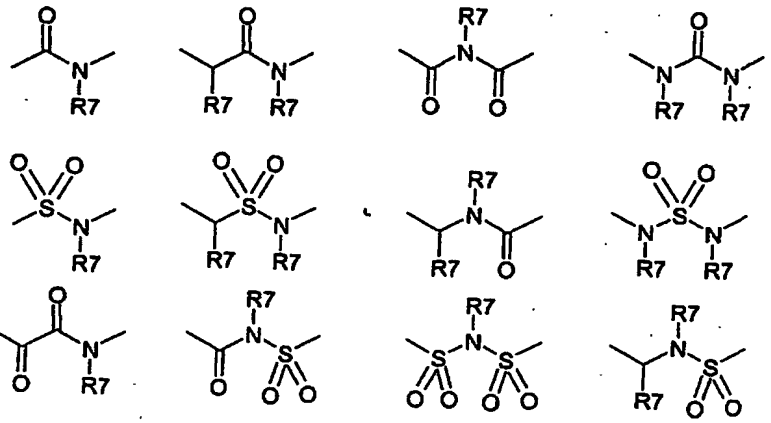
and wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined above.

In a specific embodiment X is N, R4 is hydrogen, and/or R1 is a lower straight, branched or cyclic alkyl group with 1-6 carbon atom such as, e.g., methyl, ethyl and propyl, butyl, isopropyl, isobutyl or cyclopentyl.

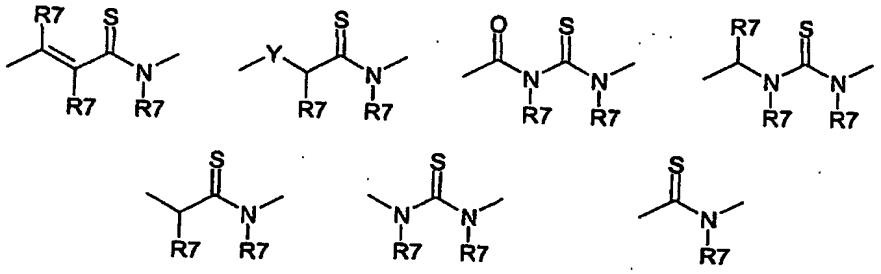
A may be selected from the group consisting of:



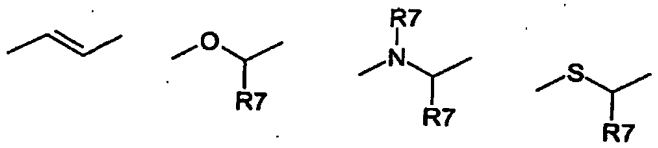
or from the group consisting of:



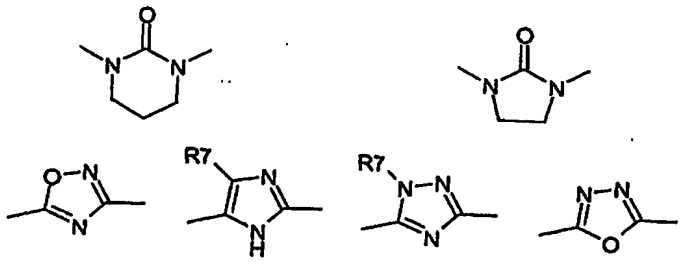
Alternatively, A is selected from the group consisting of:



or from the group consisting of:



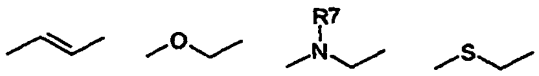
or from the group consisting of:



In particular, the quinoline compound may have the following structure:

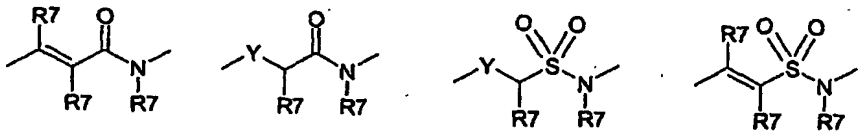
COOH or SO_2OH. Alternatively, the conversion can be made directly with the acids having A' as COOH using suitable coupling reagents such as dicyclohexylcarbodiimide (DCC), and promoters such as 1-hydroxybenzotriazole. The reverse use of A' and A'' in II and III can be applied as well to form the linker in the opposite direction.

Formation of the connecting A-linkage to form



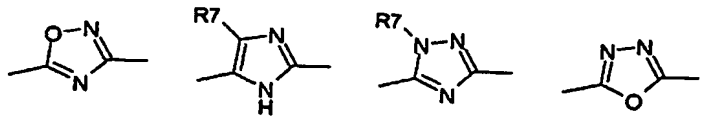
bonds in either direction between B and the quinoline can be made by N-, O- or S-alkylations of compound II with A' being OH, NH-R7, or SH with compound III with A'' being a CH_2-Lg wherein Lg being a suitable leaving group such as halogen (Cl, Br, I), tosyl or mesyl using appropriate catalysts and conditions, or by a Mitsunobu reaction with Lg being OH. The alkene linkage can be made by a Wittig reaction with compound II with A' being CHO and compound III with A'' being CH_2-PPh_3. The reverse use of A' and A'' in II and III can be applied as well to form the linker in the opposite direction.

Formation of the connecting A-linkage to form

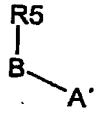


bonds in either direction between B and the quinoline can be made by N-, O- or S-alkylations of compound II with A' being OH, NH-R7, or SH with compound III with A'' being a –NR7-CO-CHR7-Lg or –NR7-SO_2-CHR7-Lg wherein Lg being a suitable leaving group such as halogen (Cl, Br, I), tosyl or mesyl using appropriate catalysts and conditions, or by a Mitsunobu reaction with Lg being OH. The alkene linkage can be made by a Horner-Emmons-Wadsworth reaction with compound II with A' being CHO. The reverse use of A' and A'' in II and III can be applied as well to form the linker in the opposite direction.

The 5-membered heterocyclic linkers



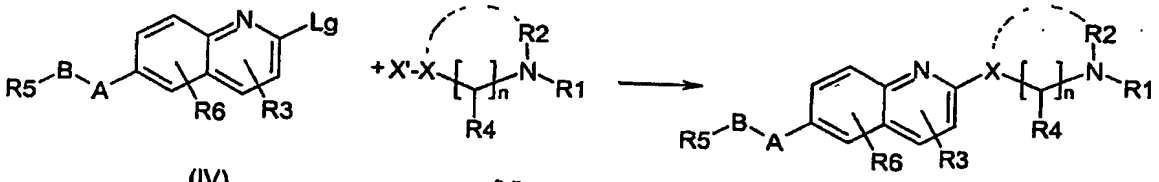
can be made according to standard cyclisation procedures using appropriate solvents, catalysts and temperatures. For example, formation of 1,2,4-triazole can be made from II with A' being acylhydrazide with III with A'' being amide or thioamide or the reverse orientation of A' and A''. 1,2,4-Oxadiazole can be formed from II with A' being amidoxime with III with A'' being carboxylic ester or the reverse orientation of A' and A''. 1,3,4-Oxadiazole can be formed from II with A' being acylhydrazide with III with A'' being carboxylic ester or the reverse orientation of A' and A''.



(II)

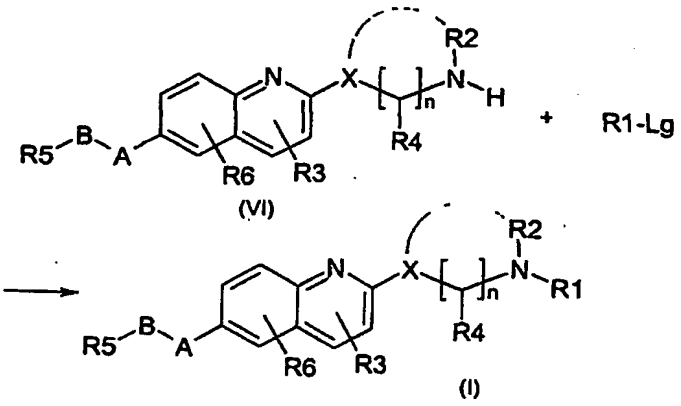
Aromatic substituents R3, R5 and R6 are preferably introduced prior to formation of the A- or B-linkage either direct or via a masked functionality that is compatible with the subsequent synthetic steps.

Compounds of forumula I can also be made by reacting a quinoline with a leaving group in the 2-position (IV) with a nucleophilic or activated fragment (V), e.g. in an aromatic nucleophilic substitution or a metal catalyzed coupling reaction.



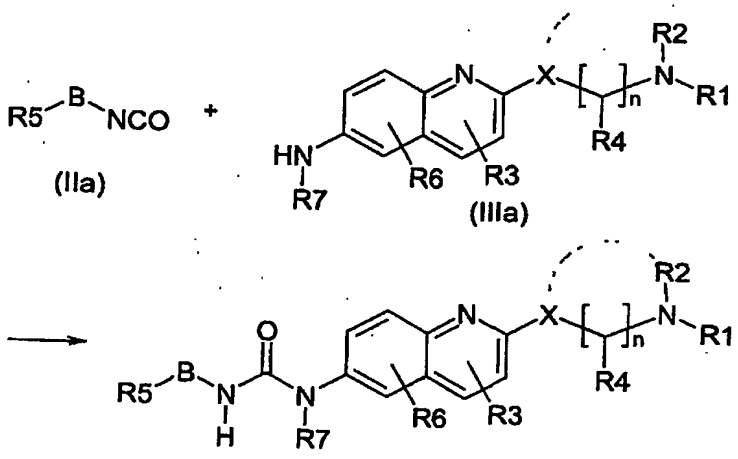
(IV) (V) (I)

Alternatively, compounds of formula I can be made by N-alkylation of compounds of formula I having R1 or R2 being hydrogen using well-known synthetic routes such as reductive alkylation or alkylation with alkyl halides in case the functionalisation of the molecule is compatible with this type of reactions. For example amines VI can be reacted with reagents R1-Lg wherein Lg being a leaving group according to the following general scheme:

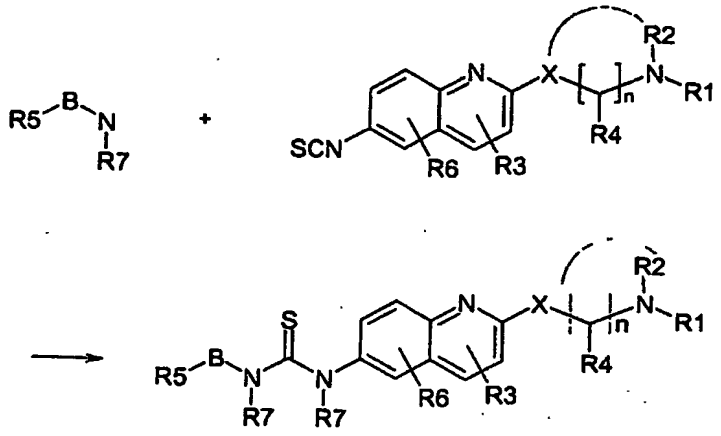


Examples of specific synthetic methods

Thus, compound I having NHCON-R7 as linker A with R7 defined as hydrogen or lower alkyl or alkenyl group, can be produced, for instance, by the following urea reaction, or by the corresponding inverse reaction, analogous to formation of the thiourea below.



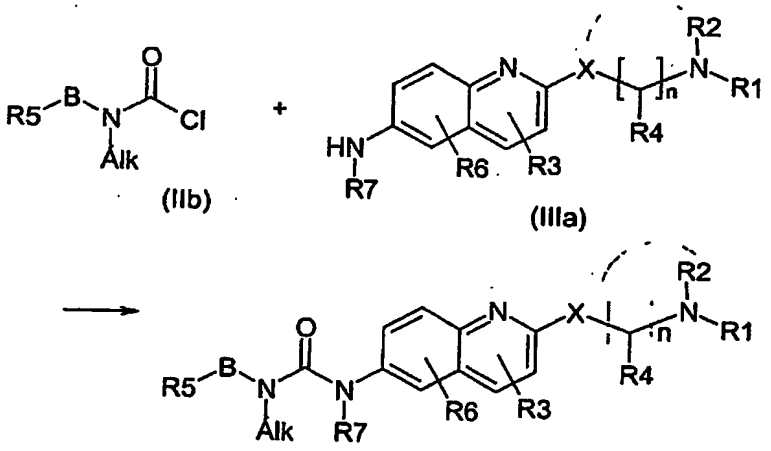
Compounds of formula I containing thioureas can be made from reactions of thioisocyanates with amines, analogous to the metods exemplified for ureas.



Compound IIa and compound IIIa are reacted in an inert solvent in accordance with standard procedures. Typically, inert solvents can be ether solvents, halogenated hydrocarbon solvents, nitrile solvents, aromatic solvents and amide solvents. Reaction temperature is usually room temperature and the reaction time is 2 hours to 1 day.

Compound IIa can be produced from the corresponding carboxylic acid. For instance, 4-phenoxyphenylisocyanate can be produced in accordance with methods such as described in "*Comprehensive Organic Transformation*", 2nd Edition (Wiley); R.C. Larock.

Compound I having NAlk-CO-NR7 as linker A with R7 defined as hydrogen or lower alkyl or alkenyl group, can be produced, for instance, by the following urea reaction.

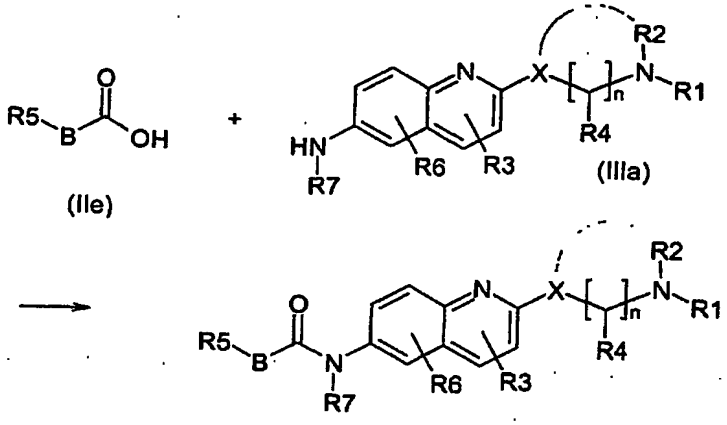


(IIb) (IIIa)

Compound IIIa and 1 equivalent of compound IIb are reacted in an inert solvent, usually in the presence of an excess of a base in accordance with known procedures (e.g. WO 9205174; *J.Med.Chem.* 43(20), 3653-3664, 2000). Suitable inert solvents can be ether

solvents, halogenated hydrocarbon solvents, nitrile solvents, aromatic solvents and amide solvents. As a base can be used for instance triethylamine, diisopropylethylamine and sodium carbonate. Typically, the reaction temperature is 0 °C to room temperature and the reaction time is 1 hour to 1 day.

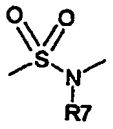
Compound I having CON-R7 as linker A with R7 defined as hydrogen or lower alkyl or alkenyl group, can be produced by the following amidation reaction.



The amide bonds are formed by reacting a suitably activated carboxylic acid IIe (acid chloride, mixed anhydrides, esters with phenol bearing electron withdrawing substituents, 1-hydroxybenzotriazole, N-hydroxysuccinimide, 2-hydroxypyridine) with anilines IIIa in an inert solvent. As inert solvents can be used ether solvents, amide solvents and halogenated hydrocarbon solvents. If required the reaction is performed in the presence of a base. Suitable bases that can be used are triethylamine, diiisopropylethylamine, pyridine, 4-dimethylaminopyridine (DMAP) and sodium carbonate. The reaction temperature is usually between 0°C to 30°C and reaction time is 1 hour to 1 day.

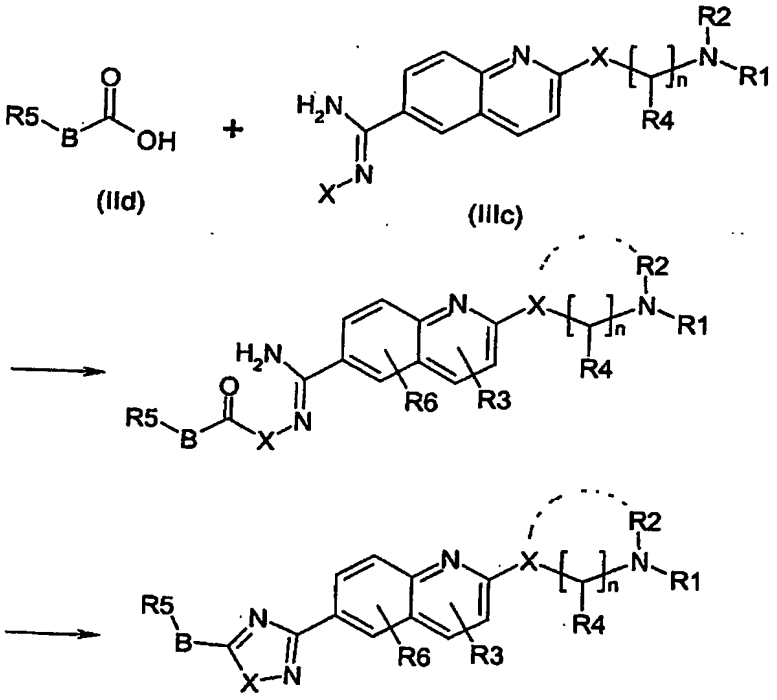
The coupling can also be performed directly from IIe using suitable coupling reagents such as dicyclohexylcarbodiimide (DCC), 1-(3-dimethylaminopropyl)-3-ethyl-cabodiimide (EDCI), N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ) preferably in presence of promoting agents capable of forming an active ester such as 1-hydroxybenzotriazole, N-hydroxysuccinimide, 2-hydroxypyridine in an inert solvent. As inert solvents can be used ether solvents, amide solvents and halogenated hydrocarbon solvents. If required the reaction is performed in the presence of a base. Suitable bases that can be used are triethylamine, diiisopropylethylamine, pyridine, N-ethyldiisopropylamine, and 4-methylmorpholine. The reaction temperature is usually between 0°C to 30°C and reaction time is 1 hour to 1 day.

Analogously, a sulphonamide group, as the connecting A-linkage to form



bonds can be made via the corresponding reaction of Ar-NH-R7 (IIIa) with activated forms of sulphonic acids, such sulphonyl chlorides, in the presence of base.

Compound I having 1,2,4-oxadiazole (X=O) or 1,2,4-triazole (X=NH) heterocyclic rings as linker A can be produced, for instance, by the following cyclodehydratation reaction.

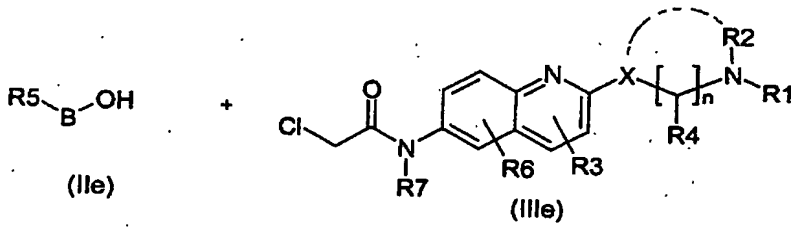


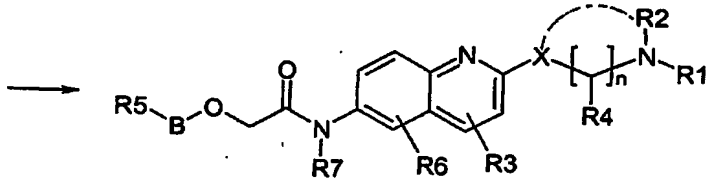
The ring closure is done in an inert solvent with or without the presence of a suitable base or acid (e.g. N-tetrabutyl ammonium fluoride, sodium hydride, sodium ethoxide or polyphosphoric acid) in accordance with standard methods such as described in *Tetrahedron Lett.* 42, 1441-1443, 2001; *Tetrahedron Lett.* 42, 1495-1498, 2001. Suitable, inert solvents can be ether solvents, amide solvents and aromatic solvents. The reaction temperature is usually room temperature to 100°C and the reaction time is 1 hour to 3 days.

The intermediate can be produced by reaction of an activated derivative of compound IId with 1 equivalent of compound IIIc in an inert solvent in the presence of a base. As inert solvents can be used ether solvents, amide solvents and halogenated hydrocarbon solvents. Suitable bases that can be used are triethylamine, diiisopropylethylamine, pyridine and sodium carbonate.

Appropriate examples of the activated derivatives of compound IId include active esters (e.g. esters with phenol bearing electron withdrawing substituents, 1-hydroxybenzotriazole, N-hydroxysuccinamide), acid chlorides, symmetrical or unsymmetrical anhydrides and orthoesters. The reaction temperature is usually between 0°C to 30°C and reaction time is 1 hour to 1 day.

Compounds of the type Ie can be made e.g. by reacting α-halo-amides of type IIIe with alcohols or phenols of type IIe.





(Ie)

The reaction may be performed by heating a solution of IIe (2.5 equiv) with IIIe in acetone, in the presence of excess of a base, such as potassium carbonate (5 equiv). The reaction temperature is usually between 20 and 60 °C, and the reaction time is usually between 0.5 and 24 hours.

Compounds

Below follows some examples of specific compounds for use according to the invention. In the compounds mentioned the different parts of the compounds, i.e. the linker –A-, the B group, the R1, R2, R3, R4, R5, R6 groups and the chain length are specified. Though not shown nor specifically mentioned, the invention also includes all compounds wherein all the mentioned variations in one part of the molecule, e.g. linker –A- is combined with all

variations of the other features mentioned in the examples.

2-(2,4-Dichloro-phenoxy)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,
3-(3-Chloro-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-p-tolyl-acrylamide
3-(2,5-Dimethoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-2-m-tolyloxy-acetamide,
3-(2,3-Dimethoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
3-[4-(3-Methyl-butoxy)-phenyl]-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
3-(4-Ethoxy-3-methoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
2-(2,4-Dichloro-phenoxy)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-propionamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3,4-dimethyl-benzamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-4-methoxy-benzamide,
4-Butyl-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-benzamide,
5-Bromo-furan-2-carboxylic acid [2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-amide,
5-Chloro-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-methoxy-benzamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3,5-dimethoxy-benzamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-(3-methoxy-phenyl)-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2,4-dimethoxy-benzamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3,4-dimethoxy-benzamide,
4-Bromo-N-[2-(4-ethyl-piperazin-1-y
l)-4-methyl-quinolin-6-yl]-3-methox
y-benzamide,
2-(3,4-Dimethoxy-phenyl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
3-(3-Chloro-phenyl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acrylamide,
3-(3-Chloro-phenyl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acrylamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-p-tolyl-acrylamide,
2-(3,4-Dichloro-phenyl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-(3-trifluoromethyl-phenyl)-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-(4-methoxy-phenyl)-propionamide,
3-(2,5-Dimethoxy-phenyl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acrylamide,

6-Chloro-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-nicotinamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-trifluoromethyl-benzamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-trifluoromethyl-benzamide,
2-(4-Bromo-5-methyl-3-trifluoromethyl-pyrazol-1-yl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
2-(4-Bromo-5-methyl-3-trifluoromethyl-pyrazol-1-yl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
2-(4-Chloro-phenoxy)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
2-(4-Chloro-phenoxy)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
2-(4-Chloro-phenoxy)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-(4-isopropoxy-phenyl)-acrylamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-(2-isopropoxy-phenyl)-acrylamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-(2-isopropoxy-phenyl)-acrylamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-(2-thioxo-benzooxazol-3-yl)-propionamide,
2-Thiophen-2-yl-quinoline-4-carboxylic acid [2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-amide,
Pyrazine-2-carboxylic acid [2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-amide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2,6-difluoro-benzamide,
2-Methyl-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
2-Chloro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-nicotinamide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-isonicotinamide,
Benzo[1,3]dioxole-5-carboxylic acid [4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-amide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-nicotinamide,
N-[4-Methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-3-trifluoromethyl-benzamide,
3-Dimethylamino-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
4-Ethoxy-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
2-Chloro-4-fluoro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
2-Fluoro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
4-tert-Butyl-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
4-Butyl-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
4-Fluoro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
2-Methoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
3,4,5-Trimethoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamideN-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-2-nitro-benzamide,

3-Chloro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
2-Chloro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
4-Bromo-3-methoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
4-Diethylamino-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
2-Chloro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-4-nitro-benzamide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-nitro-benzamide,
2,4-Dimethoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
3,4-Dimethoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
3-Methyl-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-4-nitro-benzamide,
Pyrazine-2-carboxylic acid [4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,
3-Methoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
5-Chloro-2-methoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
2-Thiophen-2-yl-quinoline-4-carboxylic acid [4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,
2-Ethoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
3,4,5-Triethoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
5-Bromo-2-chloro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
2,3-Dimethoxy-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
3-Dimethylamino-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
6-Chloro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-nicotinamide,
3-Fluoro-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-benzamide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-trifluoromethyl-benzamide,
Benzo[1,3]dioxole-5-carboxylic acid [4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,
Thiophene-2-carboxylic acid [4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,
Furan-2-carboxylic acid [4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,
5-Bromo-furan-2-carboxylic acid [4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,
2-(4-Chloro-phenyl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-(4-nitro-phenyl)-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-(4-methoxy-phenyl)-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-p-tolyl-acetamide,
2-(2-Chloro-6-fluoro-phenyl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
2-(3-Methoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-pyridin-3-yl-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-(2-methoxy-phenyl)-acetamide,

2-(4-Methoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-2-m-tolyl-acetamide,
2-(2-Methoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,
2-(3,4-Dichloro-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,
2-(3-Methoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,
2-(2-Bromo-phenyl)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
2-Cyclopentyl-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-phenyl-acetamide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-2-(3-trifluoromethyl-phenyl)-acetamide,
3-(4-Bromo-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-(4-methoxy-phenyl)-propionamide,
2-(2,4-Dichloro-phenoxy)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-propionamide,
2-(4-Chloro-phenoxy)-N-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-acetamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-(pyridin-4-ylsulfanyl)-acetamide,
3-(2,5-Dimethoxy-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-m-tolyloxy-acetamide,
3-(3,4-Dimethoxy-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
3-(4-Methoxy-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-propionamide,
3-Benzo[1,3]dioxol-5-yl-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
3-(2-Isopropoxy-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
3-(4-Methoxy-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
2-(4-Chloro-phenoxy)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acetamide,
2-Methyl-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-3-phenyl-acrylamide,
N-[4-Methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-2-(pyridin-4-ylsulfanyl)-acetamide,
3-(4-Ethoxy-3-methoxy-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

3-[4-(3-Methyl-butoxy)-phenyl]-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

3-(4-Isopropoxy-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

3-(2,3-Dimethoxy-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

N-[4-Methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-2-m-tolyloxy-acetamide,

3-(3,4-Dimethoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

3-(2-Chloro-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

2-Methanesulfonyl-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid [4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-amide,

N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-p-tolyl-acrylamide,

3-(2-Ethoxy-phenyl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

N-[4-Methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-2-(2-oxo-benzooxazol-3-yl)-acetamide,

N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-(3,4,5-trimethoxy-phenyl)-acrylamide,

2-(2,4-Dichloro-phenoxy)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,

3-(3-Chloro-phenyl)-N-[4-methyl-2-(-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

2-(2,4-Dichloro-phenoxy)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-propionamide,

3-[4-(3-Methyl-butoxy)-phenyl]-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

3-Benzo[1,3]dioxol-5-yl-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

3-(4-Methoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-propionamide,

N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-pyridin-3-yl-acrylamide,

2-Methyl-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-phenyl-acrylamide,

2-(4-Chloro-phenoxy)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,

3-(4-Methoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

3-(2,5-Dimethoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-crylamide,

N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-2-m-tolyloxy-acetamide,

3-(2,3-Dimethoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,

N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-2-(2-oxo-benzooxazol-3-yl)-acetamide,

3-(2-Isopropoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
3-(2-Isopropoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
3-(4-Ethoxy-3-methoxy-phenyl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
2-(2,4-Dichloro-phenoxy)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-propionamide,
3-Furan-2-yl-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-ac
rylamide,
3-(5-Methyl-furan-2-yl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
3-(5-Methyl-furan-2-yl)-N-[4-methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-acrylamide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-(3-methyl-thiophen-2-yl)-acrylamide,
N-[4-Methyl-2-(4-pyrimidin-2-yl-piperazin-1-yl)-quinolin-6-yl]-3-thiophen-2-yl-acrylamide,
N-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-thiophen-2-yl-acrylamide,
1-Benzo[1,3]dioxol-5-ylmethyl-3-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-thiourea,
1-(2-Ethyl-phenyl)-3-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-1-methyl-thiourea,
1-Ethyl-3-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-1-(4-fluoro-phenyl)-thiourea,
1-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-furan-2-ylmethyl-thiourea,
1-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-(4-fluoro-benzyl)-thiourea,
1-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-(2-methoxy-benzyl)-thiourea,
1-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-thiophen-2-ylmethyl-thiourea,
1-(4-Ethoxy-phenyl)-1-ethyl-3-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-thiourea,
1-Benzyl-3-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-1-methyl-thiourea,
1-(4-Ethyl-phenyl)-3-[2-(4-ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-1-propyl-thiourea,
2-(2,4-Dichloro-phenoxy)-N-(2-dimethylaminomethyl-quinolin-6-yl)-acetamide,
2-(2,4-Dichloro-phenoxy)-N-{2-[(2-dimethylamino-ethyl)-methyl-amino]-quinolin-6-yl}-acetamide,
2-(2,4-Dichloro-phenoxy)-N-[2-(2-morpholin-4-yl-ethyl)-quinolin-6-yl]-acetamide,
2-(2,4-Dichloro-phenoxy)-N-[2-(2-dimethylamino-ethoxy)-quinolin-6-yl]-acetamide,
2-(2,4-Dichloro-phenoxy)-N-{2-[(1-methyl-pyrrolidin-2-ylmethyl)-amino]-quinolin-6-yl}-acetamide,
N-[2-(4-Amino-butyl)-quinolin-6-yl]-2-(2,4-dichloro-phenoxy)-acetamide,
2-(2,4-Dichloro-phenoxy)-N-(6-dimethylaminomethyl-5,6,7,8-tetrahydro-acridin-2-yl)-acetamide,

2-(2,4-Dichloro-phenoxy)-N-{2-[2-(3,4-dihydro-1H-isoquinolin-2-yl)-cyclopentylmethyl]-quinolin-6-yl}-acetamide,

1-(4-Methyl-benzyl)-3-[2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-urea,

1-(4-Fluoro-benzoyl)-1-methyl-3-[2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-urea,

1-[2-(4-Methyl-piperazin-1-yl)-quinolin-6-yl]-ethanesulfonic acid [1-(4-chloro-phenyl)-ethyl]-amide,

2,3-Dihydro-benzo[1,4]dioxine-2-carboxylic acid [2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,

2-Phenyl-propene-1-sulfonic acid [2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,

Thiophene-2-carboxylic acid methyl-[2-(4-methyl-piperazin-1-yl)-quinoline-6-carbonyl]-amide,

2-[4-(3-Acetylamino-benzyl)-piperazin-1-yl]-quinoline-6-carboxylic acid [1-(4-fluoro-phenyl)-propyl]-methyl-amide,

C-(4-Chloro-phenoxy)-N-methyl-N-[2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-methanesulfonamide,

1-[2-(4-Methyl-piperazin-1-yl)-quinolin-6-yl]-3-(3-trifluoromethoxy-phenyl)-urea,

2-Phenyl-propene-1-sulfonic acid [4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,

1-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-(4-phenoxy-phenyl)-urea,

1-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-(4-trifluoromethoxy-phenyl)-urea,

1-(5-Methoxy-pyrazin-2-yl)-3-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-urea,

1-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-pyridin-3-ylmethyl-urea,

1-[4-Methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-3-thiophen-2-ylmethyl-urea,

2-(1H-Indol-3-yl)-N-[4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,

3,4-Dihydro-1H-isoquinoline-2-carboxylic acid [4-methyl-2-(4-propyl-piperazin-1-yl)-quinolin-6-yl]-amide,

5-Chloro-2,3-dihydro-benzofuran-2-carboxylic acid [4-methyl-2-(4-methyl-piperazin-1-yl)-quinolin-6-yl]-amide,

2-(4-Methyl-piperazin-1-yl)-6-[(2-phenyl-cyclopropanecarbonyl)-amino]-quinoline-4-carboxylic acid dimethylamide,

N-[2-(2-Diethylamino-ethylsulfanyl)-4-methyl-quinolin-6-yl]-3-furan-2-yl-acrylamide,

N-[2-(4-Ethyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-2-(1H-indol-3-yl)-2-oxo-acetamide,

3-(2,4-Dichloro-phenyl)-N-(4-methyl-2-morpholin-4-yl-quinolin-6-yl)-acrylamide,

3-Benzofuran-2-yl-N-[2-(3-dimethylamino-piperidin-1-yl)-4-methyl-quinolin-6-yl]-acrylamide,

6-Methyl-4-oxo-chroman-2-carboxylic acid {2-[(3-acetylamino-benzyl)-(2-dimethylamino-ethyl)-amino]-4-methyl-quinolin-6-yl}-amide,

N-[2-(4-Benzyl-piperazin-1-yl)-4-methyl-quinolin-6-yl]-3-(4-trifluoromethoxy-phenyl)-acrylamide,

6-Chloro-4-oxo-chroman-2-carboxylic acid [4-methyl-2-(3-pyrrolidin-1-yl-azepan-1-yl)-quinolin-6-yl]-amide,

6,8-Dichloro-4-oxo-chroman-2-carboxylic acid {2-[ethyl-(3-piperidin-1-yl-propyl)-amino]-4-methyl-quinolin-6-yl}-amide,

4-Oxo-chroman-2-carboxylic acid [2-(4-dimethylamino-piperidin-1-yl)-4-methyl-quinolin-6-yl]-amide,

Benzo[b]thiophene-3-carboxylic acid {4-methyl-2-[methyl-(2-pyrrolidin-1-yl-ethyl)-amino]-quinolin-6-yl}-amide,

3-(2-Chloro-phenyl)-N-{2-[(9H-fluoren-9-yl)-methyl-amino]-4-methyl-quinolin-6-yl}-acrylamide,

2-Phenyl-cyclopropanecarboxylic acid [2-(4-methyl-piperazin-1-yl)-4-phenyl-quinolin-6-yl]-amide,

N-{4-Ethyl-2-[methyl-(2-methylamino-cyclopentyl)-amino]-quinolin-6-yl}-3-phenyl-propionamide,

2-(4-Chloro-phenoxy)-N-[4-methyl-2-(4-methyl-3-phenyl-piperazin-1-yl)-quinolin-6-yl]-acetamide,

N-[2-(3-Amino-2-phenyl-pyrrolidin-1-yl)-4-methyl-quinolin-6-yl]-2-phenoxy-acetamide,

N-[2-(1-Ethyl-pyrrolidin-3-ylamino)-4-methyl-quinolin-6-yl]-2-methyl-3-phenyl-acrylamide,

N-[2-(2-Amino-ethylamino)-4-methyl-quinolin-6-yl]-2-phenylsulfanyl-acetamide,

N-[4-Methyl-2-(4-methyl-[1,4]diazepan-1-yl)-quinolin-6-yl]-2-pentafluorophenyloxy-acetamide

Salts, complexes or solvates

The invention also relates to the use of the compound in the form of their physiologically acceptable salts, complexes, solvates or prodrugs.

When a compound for use according to the invention possesses a basic functional group it can form a salt with an inorganic or organic acid.

Examples of physiologically acceptable salts of the compounds according to the invention include salts with inorganic acids, salts with organic acids, and salts with basic or acidic amino acids.

Examples of salts with inorganic acids include salts with hydrochloric acid, hydrobromic acid, hydroiodic acid, nitric acid or nitrous acid (to form e.g. a nitrate or a nitrite), sulfuric acid (to form e.g., a H_2SO_3 salt, a sulfate or a H_2SO_5 salt) and phosphoric acid (to form e.g. a H_3PO_3 salt or a H_3PO_4 salt)

Examples of salts with organic acids include salts with formic acid, acetic acid, propionic acid, butyric acid, pentanoic acid, longer saturated or unsaturated fatty acids, oxalic acid, tartaric acid, malonic acid, succinic acid, citric acid, $C_4H_8(COOH)_2$, $C_5H_{10}(COOH)_2$, acrylic acid, crotonic acid, maleic acid, malic acid, fumaric acid, H_2CO_3, lactic acid, ascorbic acid, benzoic acid, salicylic acid and phthalic acid, pamoic acid, trifluoroacetic acid, methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid and 3-chlorobenzoic acid.

Examples of salts with acidic amino acids include salts with aspartic acid and glutamic acid.

Optical isomers

When a compound for use according to the invention contains optical isomers, diastereomers or other stereroisomers these are included as a compound of the invention as well as the racemate, i.e. mixture of enantiomers. Each of them can be obtained by methods known by a person skilled in the art. For example the optical isomer can be obtained using an optically active synthetic intermediate, an asymmetric synthesis or subjecting the racemic mixture of the final product or a suitable intermediate to optical resolution in accordance with known methods such as, e.g., fractional recrystallisation method, chiral column method, diastereomer method etc.

Other forms

The invention also encompasses the use of a compound in amorphous, any polymorphous or any crystalline form.

Disorders

The compounds for use according to the invention can be used in medicine and modulate the activity of a MCH receptor. The compounds may be used as agents for preventing or treating diseases caused by or involving a melanin-concentrating hormone, i.e. they are

useful for treating or preventing a MCH or MCH receptor related disorder or abnormality in a subject such as, e.g., an animal or a mammal such as, e.g., a human.

The compounds for use according to the invention may have antagonistic, inverse agonistic, agonistic or allosteric activity against a MCH receptor, normally antagonistic activity.

In the present context an agonist is defined as a compound that increases the functional activity of a MCH receptor (e.g. the signal transduction through a receptor). The term "agonist" includes partial agonist, i.e. which increases the functional activity of the receptor to a submaximal level. An inverse agonist (or negative antagonist) is defined as a compound that decreases the basal functional activity of a MCH receptor. An allosteric compound is defined as a compound that enhances or diminishes the effects of other receptor ligands.

An antagonist is defined as a compound that decreases the functional activity of a MCH receptor either by inhibiting the action of an agonist or by its own intrinsic activity.

The MCH receptors mentioned in the invention include MCH1 and MCH2 receptors. It also includes MCH receptors having at least about 80% such as, e.g. at least about 85% or at least about 90% homology to the amino acid sequences CTLITAMDAN or CTIITSLDTC.

The MCH receptors may be an animal or a mammalian or non-mammalian receptor, such as a human receptor.

Increasing or decreasing the activity of a MCH receptor such as, e.g. a MCH1 receptor alleviates a MCH-related disorder or abnormality. In specific embodiments the disorder is a steroid or pituitary hormone disorder, an epinephrine release disorder, a gastrointestinal disorder, a cardiovascular disorder, an electrolyte balance disorder, hypertension, diabetes, a respiratory disorder, asthma, a reproductive function disorder, a muscoskeletal disorder, a neuroendocrine disorder, a cognitive disorder, a memory disorder such as, e.g., Alzheimer's disease, a sensory modulation and transmission disorder, a motor coordination disorder, a sensory integration disorder, a motor integration disorder, a dopaminergic function disorder such as, e.g. Parkinson's disease, a sensory transmission disorder, an olfaction disorder, a sympathetic innervation disorder, an affective disorder such as, e.g. depression, a stress-related disorder, a fluid-balance disorder, a urinary

disorder such as, e.g., urinary incontinence, a seizure disorder, pain, psychotic behaviour such as, e.g., schizophrenia, morphine or opioid tolerance, opiate addiction or migraine.

More specifically, the compounds of the invention are useful for the treatment or prevention of feeding disorders such as, e.g., overweight, adiposity, obesity and bulimia (e.g. malignant mastocytosis, exogeneous obesity, hyperinsulinar obesity, hyperplasmic obesity, hypophyseal adposity, hypoplasmic obesity, hypophysal adiposity, hypoplasmic obesity, hypothyroid obesity, hypothalamic obesity, symptomatic obesity, infantile obesity, upper body obesity, alimentary obesity, hypogonadal obesity, systemic mastocytosis, simple obesity, central obesity etc.), hyperfagia, emotional disorders, dementia or hormonal disorders.

In the present context the term body mass index or BMI is defined as body weight (kg)/height^2 (m^2), and the term overweight is intended to indicate a BMI in a range from about 25 to about 29.9, whereas obesity is intended to indicate a BMI, which is at least about 30.

A compound of the invention is also useful as an agent for preventing or treating lifestyle diseases such as, e.g., diabetes, diabetic complications (e.g. retinopathy, neuropathy, nephropathy etc.), arteriosclerosis and gonitis.

The present invention further relates to a cosmetic method for reducing overweight and/or for treating of and/or preventing overweight, bulimia, bulimia nervosa, obesity and/or complications thereto, the method comprising administering to an animal such as, e.g. a human in need thereof, an effective amount of a compound according to the invention

The invention also relates to a method for the treatment and/or prophylaxis of diseases caused by a melanin-concentrating hormone, the method comprising administering to a mammal in need thereof an efficient amount of a compound according to the invention.

A mentioned above, the MCH-related disorders may be a feeding disorder. Accordingly, the invention relates to a method for the treatment and/or prophylaxis of diseases caused by feeding disorders, the method comprising administering to a mammal in need thereof an efficient amount of a compound according to the invention.

The invention also relates to a method for modifying the feeding behaviour of a mammal, the method comprising administering to a mammal in need thereof an efficient amount of a compound according to the invention.

Furthermore, the invention relates to a method for the reduction of body mass, the method comprising administering to a mammal in need thereof an efficient amount of a compound according to the invention.

Moreover, the invention relates to a method for the treatment and/or prophylaxis of Syndrome X (metabolic syndrome) or any combination of obesity, insulin resistance, dyslipidemia, impaired glucose tolerance and hypertension, the method comprising administering to a mammal in need thereof an efficient amount of a compound according to the invention.

Another aspect of the invention is a method for the treatment and/or prophylaxis of Type II diabetes or Non Insulin Dependent Diabetes Mellitus (NIDDM), the method comprising administering to a mammal in need thereof an efficient amount of a compound according to the invention.

A still further aspect of the invention is a method for the treatment and/or prophylaxis of bulimia, bulimia nervosa and/or obesity, the method comprising administering to a mammal in need thereof an efficient amount of a compound according to the invention.

Moreover, the invention relates to a method for the treatment and/or prophylaxis of depression and/or anxiety, the method comprising administering to a mammal in need thereof an efficient amount of a compound according to the invention.

Pharmaceutical compositions

The compounds for use in the methods according to the invention are normally presented in the form of a pharmaceutical or a cosmetic composition comprising the specific compound or a physiologically acceptable salt thereof together with one or more physiologically acceptable excipients.

The compounds may be administered to the animal including a mammal such as, e.g., a human by any convenient administration route such as, e.g., the oral, buccal, nasal, ocular, pulmonary, topical, transdermal, vaginal, rectal, ocular, parenteral (including *inter*

alia subcutaneous, intramuscular, and intravenous), route in a dose that is effective for the individual purposes. A person skilled in the art will know how to chose a suitable administration route.

The pharmaceutical or cosmetic composition comprising a compound according to the invention may be in the form of a solid, semi-solid or fluid composition.

The solid composition may be in the form of tablets such as, e.g. conventional tablets, effervescent tablets, coated tablets, melt tablets or sublingual tablets, pellets, powders, granules, granulates, particulate material, solid dispersions or solid solutions.

A semi-solid form of the composition may be a chewing gum, an ointment, a cream, a liniment, a paste, a gel or a hydrogel.

The fluid form of the composition may be a solution, an emulsion including nano-emulsions, a suspension, a dispersion, a liposomal composition, a spray, a mixture, a syrup or a aerosol.

Fluid compositions, which are sterile solutions or dispersions can be utilized by for example intraveneous, intramuscular, intrathecal, epidural, intraperitoneal or subcutaneous injection of infusion. The compounds may also be prepared as a sterile solid composition, which may be dissolved or dispersed before or at the time of administration using e.g. sterile water, saline or other appropriate sterile injectable medium.

Other suitable dosages forms of the pharmaceutical compositions according to the invention may be vagitories, suppositories, plasters, patches, tablets, capsules, sachets, troches, devices etc.

The dosage form may be designed to release the compound freely or in a controlled manner e.g. with respect to tablets by suitable coatings.

The pharmaceutical composition may comprise a therapeutically effective amount of a compound according to the invention.

The content of a compound of the invention in a pharmaceutical composition of the invention is e.g. from about 0.1 to about 100% w/w of the pharmaceutical composition.

The pharmaceutical or cosmetic compositions may be prepared by any of the method well known to a person skilled in pharmaceutical or cosmetic formulation.

In pharmaceutical or cosmetic compositions, the compounds are normally combined with a pharmaceutical excipient, i.e. a therapeutically inert substance or carrier.

The carrier may take a wide variety of forms depending on the desired dosage form and administration route.

The pharmaceutically or cosmetically acceptable excipients may be e.g. fillers, binders, disintegrants, diluents, glidants, solvents, emulsifying agents, suspending agents, stabilizers, enhancers, flavours, colors, pH adjusting agents, retarding agents, wetting agents, surface active agents, preservatives, antioxidants etc. Details can be found in pharmaceutical handbooks such as, e.g., Remington's Pharmaceutical Science or Pharmaceutical Excipient Handbook.

Dosage

Optimal dosages to be administered may be determined by those skilled in the art, and will vary with the particular compound in use, the strength of the composition, the route of administration, the frequency of administration, the age, weight, gender, diet and condition of the subject to be treated and the condition being treated and the advancement of the disease condition etc.

Suitable dosages may be from about 0.001 mg to about 1 g such as, e.g. from about 0.005 to about 750 mg, from about 0.01 to about 500 mg, from about 0.05 to about 500 mg, from about 0.1 to about 250 mg, from about 0.1 to about 100 mg or from about 0.5 to about 50 mg.

The amounts can be divided into one or several doses for administration daily, every second day, weekly, every two weeks, monthly or with any other suitable frequency. Normally, the administration is daily.

A compound or a pharmaceutical composition for use according to the invention may be used in combination with other drug substances such as agents for treating disorders like

e.g. diabetes, diabetes complications, obesity, hypertension, hyperlipidemia, arteriosclerosis, arthritis, anxiety, and/or depression etc.

Other aspects of the invention

The above-mentioned formulas encompass known as well as novel compounds. With respect to the novel compounds, the invention also relates to the compounds *per se* as well as to the use of the novel compounds in medicine especially the use in the prevention, treatment and/or diagnosis of the above-mentioned conditions. The details and particulars mentioned above apply *mutatis mutandis* to the other aspects of the invention.

Experimental

Materials and methods

Transfections and Tissue Culture - The cDNA encoding the human MCH-1 receptor was cloned from a human brain cDNA library and cloned into the eukaryotic expression vector pcDNA3.1 (Invitrogen). Assays were performed on transiently transfected COS-7 cells or stably transfected CHO (Chinese Hamster Ovary) cells, expressing the human MCH-1 receptor in pcDNA3.1. Stable MCH-1 receptor transfectants of CHO cells were obtained using 5 μg plasmid cDNA and a standard calcium phosphate transfection method (Johansen *et al.*, 1990; Gether *et al.*, 1992) with subsequent selection in 1 mg/ml G418 (Life Technology). Clones were screened by a MCH receptor radioligand binding assay (as described below). Stably transfected CHO cells were maintained in RPMI 1640 culture medium (Invitrogen), supplemented with 10 % fetal calf serum (Invitrogen), 100 U/ml penicillin, 100 μg/ml streptomycin (Life Technology), and 500 μg/ml G418 (Life Technology). COS-7 cells were grown in Dulbecco's modified Eagle's medium (DMEM) 1885 (Invitrogen) supplemented with 10 % fetal calf serum, 100 U/ml penicillin, 100 μg/ml streptomycin, and were transiently transfected by a standard calcium phosphate transfection method (Johansen *et al.*, 1990; Gether *et al.*, 1992) two days before assay.

Radioligand Binding Assay -Transiently transfected COS-7 cells or stably transfected CHO cells, expressing human MCH-1 receptor were seeded in multi-well culture plates one day before the assay. The number of cells per well was determined by the apparent expression efficiency of the cell line aiming at 5 - 10 % binding of the added radioligand. Cells were assayed by competition binding for 3 hours at room temperature using 15 pM

[^{125}I]-MCH (Amersham Pharmacia Biotech) plus variable amounts of unlabeled ligand in 0.5 ml of a 25 mM Hepes buffer, pH 7.4, supplemented with 10 mM $MgCl_2$, 5 mM $MnCl_2$, 10 mM NaCl, 0.1 % (w/v) bovine serum albumin (BSA), 100 µg/ml bacitracin. The assay was performed in duplicate. Nonspecific binding was determined as the binding in the presence of 1 μM MCH (Bachem). Binding data were analyzed and IC_{50} values determined by non-linear regression using the Prism software (GraphPad software, San Diego). Values of the dissociation and inhibition constants (K_d and K_i) were estimated from competition binding using the equations $K_d=IC_{50}-L$ and $K_i=IC_{50}/(1+L/K_d)$, respectively, where L is the concentration of radioligand.

Phosphatidylinositol assay - To assay phosphatidylinositol turnover, transiently transfected COS-7 cells or stably transfected CHO cells, expressing human MCH-1 receptor ($2x10^5$ cells/well) were incubated for 24 h with 5 μCi of [^{3}H]-*myo*-inositol (Amersham Pharmacia Biotech) in 0.5 ml inositol-free culture medium. Cells were washed twice in PI-buffer: 20 mM HEPES, pH 7.4, supplemented with 140 mM NaCl, 5 mM KCl, 1 mM $MgSO_4$, 1 mM $CaCl_2$, 10 mM glucose, 0.02% (w/v) bovine serum; and were incubated in 0.5 ml PI-buffer supplemented with 10 mM LiCl at 37 °C for 45 min. Phosphatidylinositol turnover was stimulated by submaximal concentrations of MCH, i.e. 10 nM in the presence of increasing amounts of ligand. The ligand was added 5 min. before adding the agonist (MCH). Cells were extracted with 10 mM ice-cold Formic acid, and the generated [^{3}H]-inositol phosphates were purified on Bio-Rad AG 1-X8 anion-exchange resin. Determinations were made in duplicate. PI data were analyzed and IC_{50} values determined by non-linear regression using the Prism software (GraphPad software, San Diego).

Scintillation Proximity Assay (SPA) – Measurement of [^{125}I]-MCH binding was performed in duplicates by incubating membranes and beads with tracer in the presences of various concentrations of test compounds (10^{-8} to 10^{-4} M) in DMSO (3 µl) at room temperature for two hours. Membranes and beads were pre-incubated for 20 min. The binding buffer contained 50 mM Tris (pH 7.4), 8 mM MgCl2, 12% glycerol, 0.1% (w/v) bovine serum albumin (BSA), and protease inhibitors (Complete protease inhibitor cocktail tablets, Roche). A final [^{125}I]-MCH (2000 Ci/mmol; Amersham Pharmacia Biotech) concentration of 75.000 cpm/well (33.8 nCi) was applied and PEI-treated WGA-coupled PVT SPA beads, type B from Amersham Pharmacia Biotech were used at a final concentration of 0.4 mg/well. Moreover, CHO-K1 membranes expressing the hMCH receptor were purchased from Euroscreen (ES-370-M) and a final concentration of 2µg/well were used. Binding data were analyzed and IC_{50} values determined by non-linear regression using the Prism

software (GraphPad software, San Diego). Values of the inhibition constant (K_i) were estimated from competition binding using the equation $K_i=IC_{50}/(1+L/K_d)$, where L and K_d are the concentration and affinity constant, respectively, of the radioligand.

References:

Gether, U., Marray, T., Schwartz, T.W., and Johansen, T.E. (1992). Stable expression of high affinity NK_1 (substance P) and NK_2 (neurokinin A) receptors but low affinity NK_3 (neurokinin B) receptors in transfected CHO cells. *FEBS Lett.*, 296, 241-244.

Johansen, T.E., Schøller, M.S., Tolstoy, S. and Schwartz, T.W. (1990). Biosynthesis of peptide precursors and protease inhibitors using new constitutive and inducible eukaryotic expressions vectors. *FEBS Lett.*, 267, 289-294.

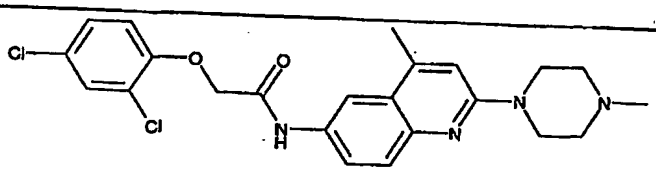
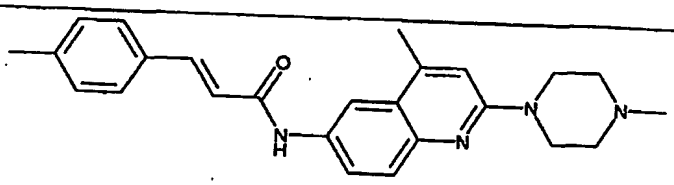
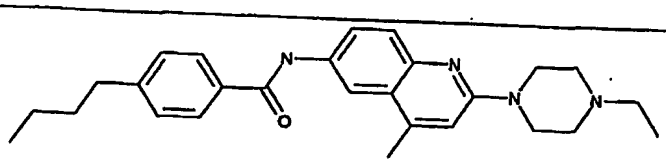
Examples

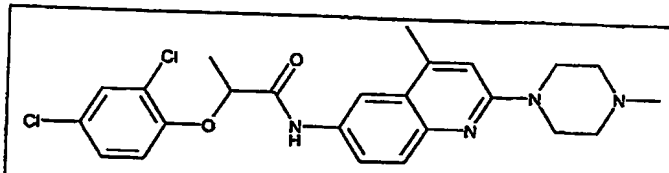
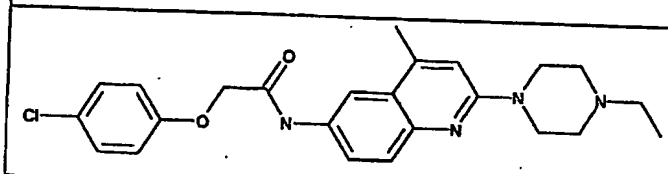
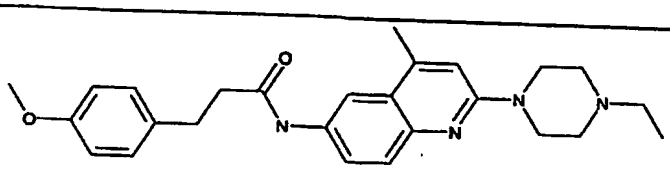
***In vitro* tests of compounds according to the invention**

The following results were obtained

The compounds in the examples can be prepared by the general synthetic methods described above.

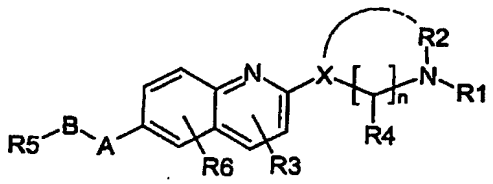
Receptor binding data

Compound	Example	Receptor binding IC50 nM	IP3 IC50 nM
	Example 1	12	72
	Example 2	20	
	Example 3	110	

	Example 4	280	2000
	Example 5	24	140
	Example 6	250	420

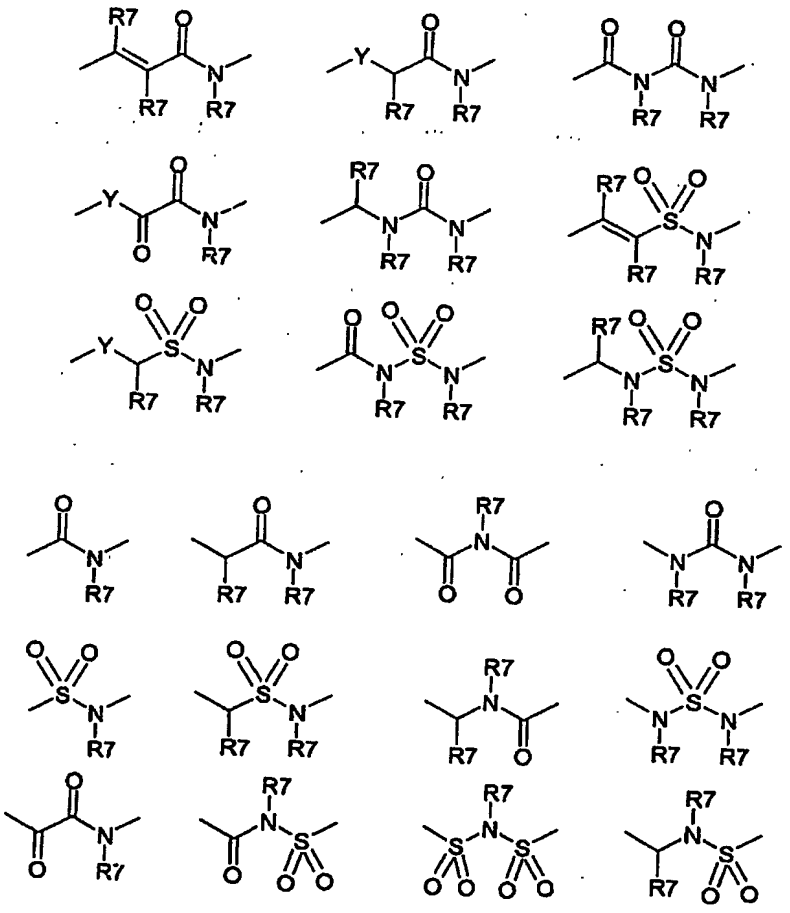
CLAIMS

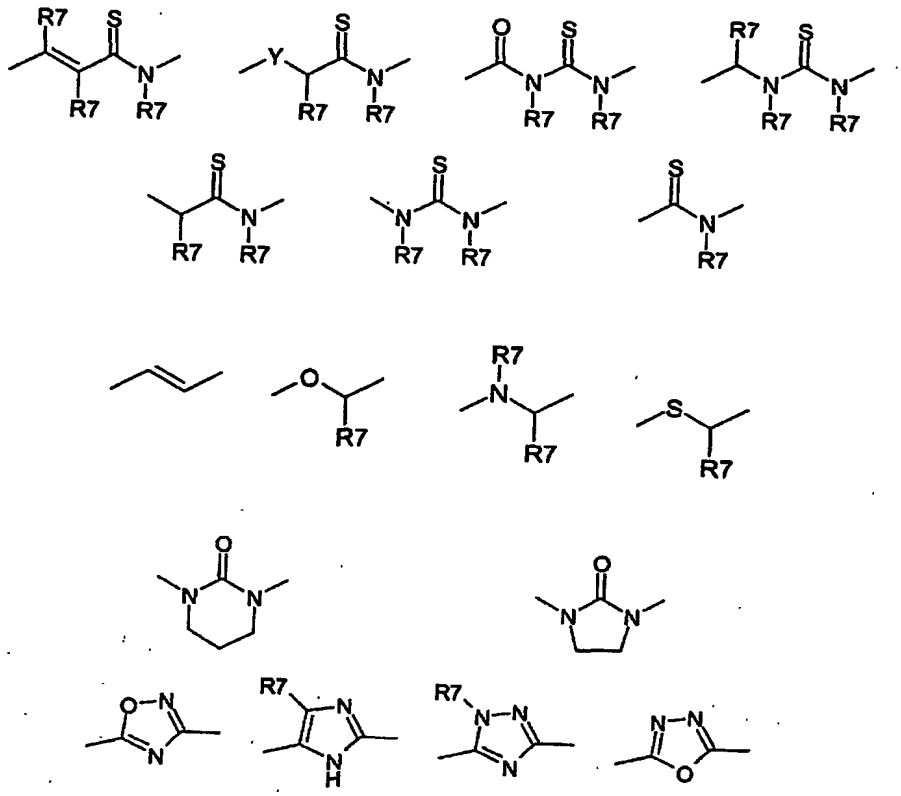
1. Use of a compound with the following structure (Formula 1a)



wherein the quinoline moiety may contain more than one nitrogen atom such as, e.g. 2 or 3 nitrogen atoms,

and wherein -A- is a linker, which is selected from the group consisting of





and, wherein the linker may be attached via either of the two free bonds to the B group;

and Y being CHR7, O, S, NR7;

and R7 is the same or different and is hydrogen or a straight or branched C_1-C_4 alkyl or alkenyl group; R7 can be linked direct or via hetero atoms to B or the quinoline ring system when chemically feasible;

and X being nitrogen, carbon, oxygen or sulphur and X being restricted to nitrogen or carbon when X linked to R2 as indicated in formula Ia;

B is an aryl or heteroaryl group such as, e.g. phenyl, pyridine, pyrimidine, pyrazine, thiophene, oxazole, isothiazole, pyrazole, pyrrole, imidazole, indole, benzimidazole, quinoline, isoquinoline, furan, benzofuran, benzothiophene, benzothiazole, indazole, thiazole, isoxazole, oxadiazole, indan;

R1 and R2 are the same or different selected from hydrogen, straight or branched alkyl, alkenyl or alkynyl groups with 1-6 carbon atoms; cycloalkyl groups with 3-7 carbons;

alkylcycloalkyl with 4-8 carbons atoms; alkylaryl groups such as benzyl, 2-ethylphenyl, 3-propylphenyl; alkylheteroaryl groups; the alkyl, aryl and heteroaryl groups may be substituted with substituents such as Alk-CONH-, Alk-O-, HO-, NC-, AlkNH-, Alk_2N-, -$CONH_2$, -CONHAlk, -$CONAlk_2$, or the aryl and heteroaryl groups fused with moieties such as -O-CH_2-O-, -N=CH-NH-, -O-CH=N-;

Alk is the same or a different alkyl, alkenyl or alkynyl group;

R4 is the same or different and is hydrogen or a straight or branched C_1-C_4 alkyl group;

R3 may be selected from hydrogen, alkyl, alkenyl or alkynyl groups, halogen atoms, alkoxy groups (AlkO-), hydroxy, alkylamino groups (AlkNH-), dialkylamino groups (Alk_2N-), hydroxylalkyl groups, carboxamido groups (-$CONH_2$, -CONHAlk, -$CONAlk_2$), acylamido groups (-NHCO-Alk), acyl groups (-CO-Alk), -CHO, nitrile, -SCH_3, partially or fully fluorinated alkyl, alkoxy or thioalkoxy groups such as -CH_2CF_3, -CF_2CF_3, -CF_3, -OCF_3, -SCF_3; -SO_2NH_2, -SO_2NHAlk, -SO_2NAlk_2, -SO_2Alk;

R1, R2, R3 or R4 may optionally be linked to each other, when possible; and oxygen or nitrogen atoms may be inserted in the chain or ring in a chemically stable position;

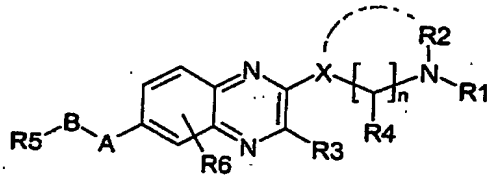
R5 is hydrogen, halogen atoms, alkyl, alkenyl or alkynyl groups, cycloalkyl groups with 3-7 carbons, aryl groups (Ar), heteroaryl groups, heterocyclyl groups, alkylcycloalkyl groups, alkylaryl groups, alkylheterocyclyl groups, alkylheteroaryl groups, arylalkoxy groups (e.g. $ArCH_2O$-), aryloxy groups (ArO-), arylamino groups (Ar-NR7-, ArNH-), arylalkylamino groups (ArAlkNH-, ArAlkNR7-, $ArCH_2NR7$-, $ArCH_2NH$-), alkoxy groups (AlkO-), alkylamino groups (AlkNH-), dialkylamino groups (Alk_2N-), -$CONH_2$, -CONHAlk, -CONHAr -$CONAlk_2$, -NHCO-Alk, -NHCO-Ar, -CO-Alk, -CO-Ar, -CF_2-Ar, -$N(CF_3)_2$, -SCH_3, partially or fully fluorinated alkyl, alkoxy or thioalkoxy groups such as -CH_2CF_3, -CF_2CF_3, -CF_3, -OCF_3, -SCF_3;

optionally, one or more R5 may be present on B; and

n is 0, 1, 2 or 3 with the proviso that
when n is 0 or 1 then X is C and
when n is 2 or 3, then X is C, O, S or N

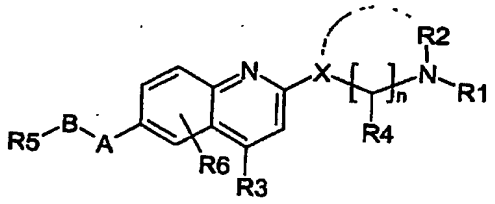
for the preparation of a pharmaceutical composition for the treatment, prophylaxis and/or diagnosis of a condition caused by or involving a melanin-concentration hormone.

2. Use according to claim 1, wherein the compound has the following structure (Formula 1b)



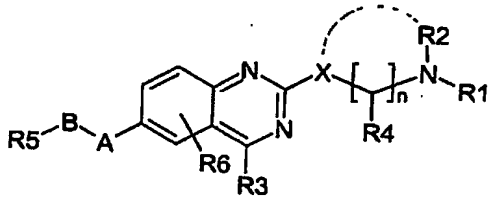
wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y, X and n are as defined in claim 1.

3. Use according to claim 1, wherein the compound has the following structure:



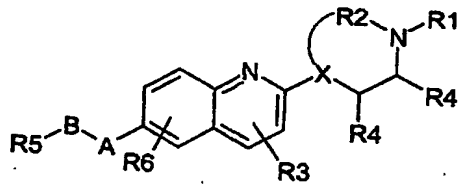
wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y, X and n are as defined in claim 1.

4. Use according to claim 1, wherein the compound has the following structure (Formula 1c)



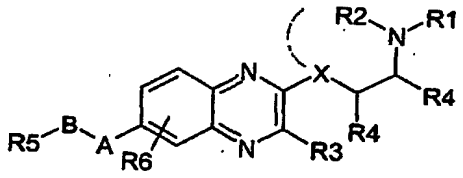
wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y, X and n are as defined in claim 1.

5. Use according to claim 1 with the following structure



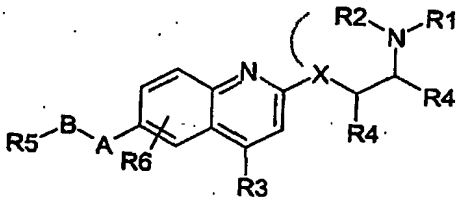
wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined in claim 1.

6. Use according to claim 2, wherein the compound has the following structure:



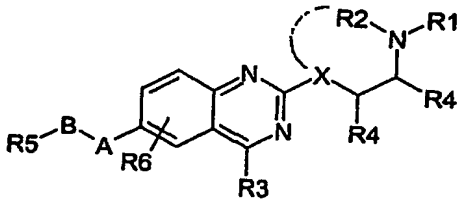
and wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined in claim 1.

7. Use according to claim 5, wherein the compound has the following structure:



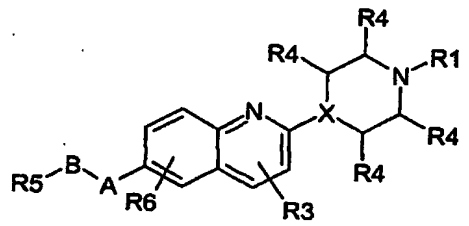
and wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined in claim 1.

8. Use according to claim 4, wherein the compound has the following structure:



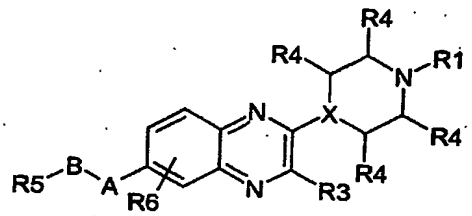
and wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined in claim 1.

9. Use according to claim 1, wherein the compound has the following structure:



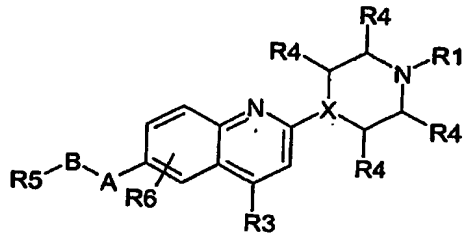
and wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined in claim 1.

10. Use according to claim 2, wherein the compound has the following structure:



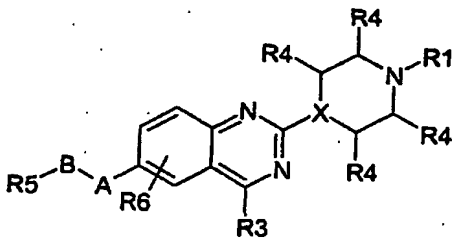
and wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined in claim 1.

11. Use according to claim 1, wherein the compound has the following structure:



and wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined in claim 1.

12. Use according to claim 4, wherein the compound has the following structure:



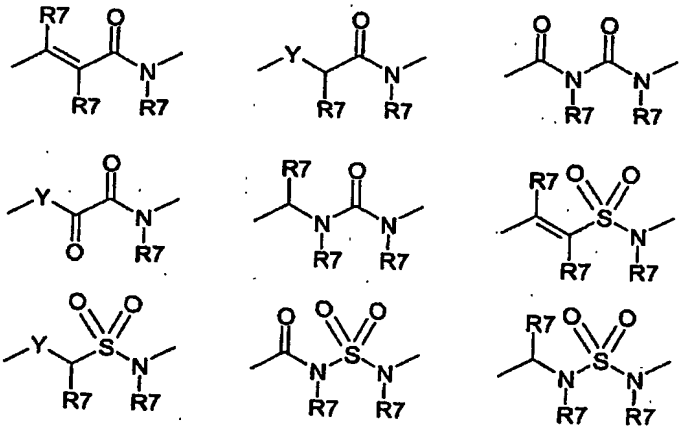
and wherein A, B, R1, R2, R3, R4, R5, R6, R7, Y and X are as defined in claim 1.

13. Use according to any of the preceding claims, wherein X is N.

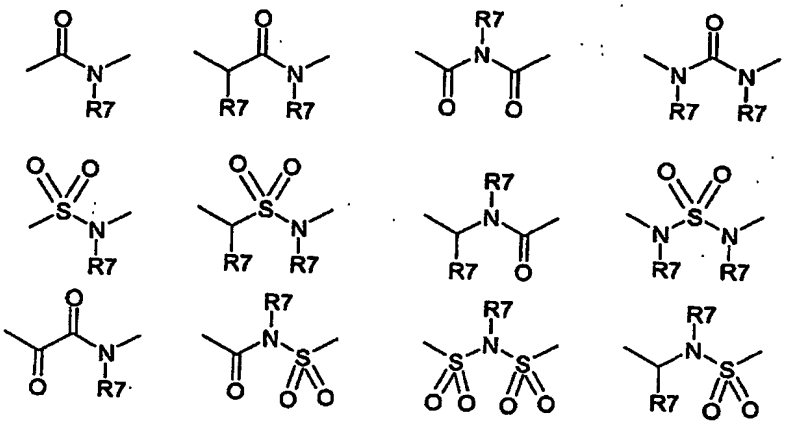
14. Use according to any of claims 9-13, wherein R4 is hydrogen

15. Use according to any of the preceding claims, wherein R1 is a lower straight, branched or cyclic alkyl group with 1-6 carbon atom such as, e.g., methyl, ethyl and propyl, butyl, isopropyl, isobutyl, cyclopentyl.

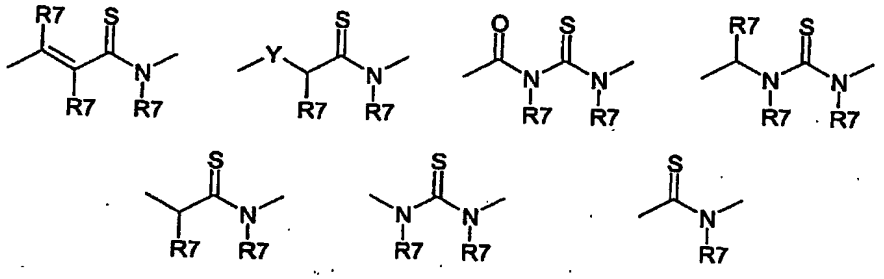
16. Use according to any of the preceding claims, wherein A is selected from the group consisting of:



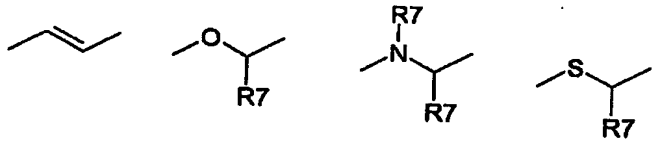
17. Use according to any of claims 1-15, wherein A is selected from the group consisting of:



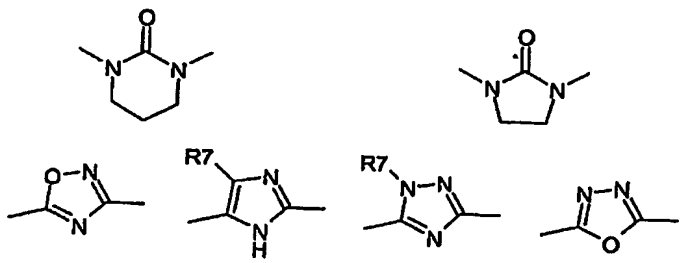
18. Use according to any of claims 1-15, wherein A is selected from the group consisting of:



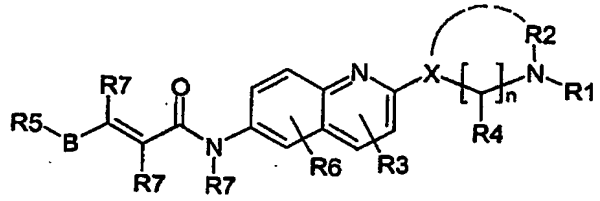
19. Use according to any of claims 1-15, wherein A is selected from the group consisting of:



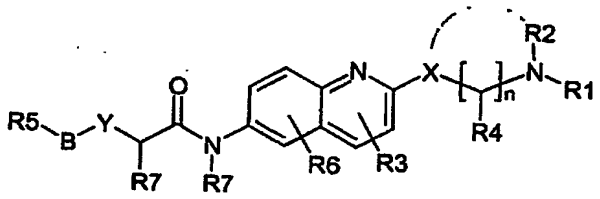
20. Use according to any of claims 1-15, wherein A is selected from the group consisting of:



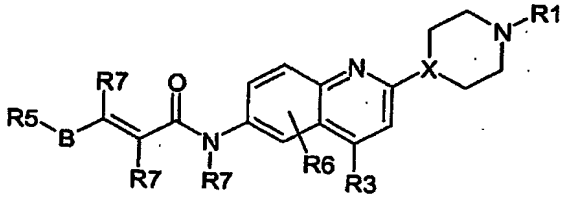
21. Use according to any of claims 1-16, wherein the compound has the following structure:



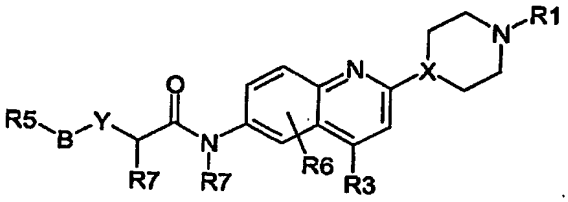
22. Use according to any of claims 1-16, wherein the compound has the following structure:



23. Use according to claims 1-16, wherein the compound has the following structure:



24. Use according to claims 1-16, wherein the compound has the following structure:



25. Use according to claim 21-24, wherein R6 is hydrogen.

26. Use according to claim 21-25, wherein R3 is methyl.

27. Use according to claim 21-26, wherein X is nitrogen.

28. Use according to claim 21-27, wherein R7 is hydrogen.

29. Use according to claim 21-28, wherein R1 is methyl or ethyl.

30. Use according to claim 22, 24-29, wherein Y is oxygen.

31. Use according to claim 21-30, wherein B is a monocyclic aryl or heteroaryl group.

32. Use according to claim 21-31, wherein B is phenyl, pyridine, pyrimidine, pyrazine, thiophene or furan.

33. Use according to claim 21-32, wherein R5 is halogen atoms, alkyl or alkenyl groups, cycloalkyl groups with 3-7 carbons, heterocyclyl groups, alkylcycloalkyl groups, alkoxy groups (AlkO-), alkylamino groups (AlkNH-), dialkylamino groups (Alk_2N-), -CONHAlk, -$CONAlk_2$, -NHCO-Alk, -CO-Alk, -$N(CF_3)_2$, -SCH_3, partially or fully fluorinated alkyl, alkoxy or thioalkoxy groups such as -CH_2CF_3, -CF_2CF_3, -CF_3, -OCF_3, -SCF_3;

34. Use according to any of the preceding claims, wherein the compound is in amorphous or crystalline form.

35. Use according to any of the preceding claims, wherein the compound is in racemic or enantiomeric form.

36. Use according to any of the preceding claims, wherein the compound is in the form of a physiologically acceptable salt, complex, solvate or prodrug thereof.

37. Use according to any the preceding claims for the preparation of a composition for preventing or treating diseases caused by or involving a melanin-concentrating hormone.

38. Use according to any of the preceding claims for the preparation of a composition for modulating the activity of a MCH receptor.

39. Use according to any of the preceding claims for the preparation of a composition that has antagonistic activity against a MCH receptor.

40. Use according to any claim 1-38 for the preparation of a composition that has agonistic, inverse agonistic or allosteric activity against a MCH receptor.

41. Use according to any of the preceding claims, wherein the MCH receptor has at least about 80% such as, e.g. at least about 85% or at least about 90% homology to the amino acid sequence CTLITAMDAN or CTIITSLDTC

42. Use according to any of the preceding claims, wherein the MCH receptor comprises the amino acid sequence CTLITAMDAN or CTIITSLDTC.

43. Use according to any of the preceding claims, wherein the MCH receptor is a MCH1 or MCH2 receptor.

44. Use according to any of the preceding claims, wherein the MCH receptor is a MCH1 receptor.

45. Use according to any of the preceding claims, wherein the MCH receptor is a mammalian receptor such as human receptor.

46. Use according to any of the preceding claims for the preparation of a composition for preventing or treating feeding disorders.

47. Use according to any of claims 1-38 or 40-46 for the preparation of a composition for reducing body mass.

48. Use according to any of claims 1-38 or 40-47 for the preparation of a composition for preventing or treating Syndrome X (metabolic syndrome), or any combination of obesity, insulin resistance, dyslipidemia, impaired glucose tolerance and hypertension.

49. Use according to any of claims 1-38 or 40-48 for the preparation of a composition for preventing or treating Type II diabetes or Non Insulin Dependent Diabetes Mellitus (NIDDM).

50. Use according to any of claims 1-38 or 40-49 for the preparation of a composition for preventing or treating bulimia, obesity and/or bulimia nervosa.

51. Use according to any of claims 1-45, which is an antidepressant and/or anti-anxiety agent.

52. A cosmetic method for reducing overweight and/or for treating of and/or preventing overweight, bulimia, bulimia nervosa, obesity and/or complications thereto, the method comprising administering to an animal such as, e.g. a human in need thereof, an effective amount of a compound defined in any of claims 1-38 or 40-51.

53. A method for the treatment and/or prophylaxis of diseases caused by a melanin-concentrating hormone, the method comprising administering to a mammal in need thereof an efficient amount of a compound defined in any of claims 1-36.

54. A method for the treatment and/or prophylaxis of diseases caused by feeding disorders, the method comprising administering to a mammal in need thereof an efficient amount of a compound defined in any of claims 1-36.

55. A method for modifying the feeding behaviour of a mammal, the method comprising administering to a mammal in need thereof an efficient amount of a compound defined in any of claims 1-36.

56. A method for the reduction of body mass, the method comprising administering to a mammal in need thereof an efficient amount of a compound defined in any of claims1-38 or 40-50.

57. A method for the treatment and/or prophylaxis of Syndrome X (metabolic syndrome) or any combination of obesity, insulin resistance, dyslipidemia, impaired glucose tolerance and hypertension, the method comprising administering to a mammal in need thereof an efficient amount of a compound defined in any of claims 1-38 or 40-50.

58. A method for the treatment and/or prophylaxis of Type II diabetes or Non Insulin Dependent Diabetes Mellitus (NIDDM), the method comprising administering to a mammal in need thereof an efficient amount of a compound defined in any of claims 1-38 or 40-50.

59. A method for the treatment and/or prophylaxis of bulimia, bulimia nervosa and/or obesity, the method comprising administering to a mammal in need thereof an efficient amount of a compound defined in any of claims 1-38 or 40-50.

68. A pharmaceutical composition according to claim 65 in fluid form, wherein the composition is in the form of a solution, an emulsion, a suspension, a dispersion, a liposomal composition, a spray, a mixture, or a syrup.

69. A pharmaceutical composition according to any of claims 61-68 comprising a therapeutically effective amount of a compound according to claims.

70. A pharmaceutical composition according to claim 69, wherein the amount is from about 0.001 mg to about 1 g such as, e.g. from about 0.005 to about 750 mg, from about 0.01 to about 500 mg, from about 0.05 to about 500 mg, from about 0.1 to about 250 mg, from about 0.1 to about 100 mg or from about 0.5 to about 50 mg.